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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,711	01/17/2002	Yunxiang Zhu	ZHUY 8216US	8638
1688	7590	04/16/2004	EXAMINER	
POLSTER, LIEDER, WOODRUFF & LUCCHESI 12412 POWERSCOURT DRIVE SUITE 200 ST. LOUIS, MO 63131-3615			KHARE, DEVESH	
			ART UNIT	PAPER NUMBER

1623

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/051,711

Applicant(s)

ZHU, YUNXIANG

Examiner

Devesh Khare

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5, 6, 8-15 and 22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5, 6, 8-15 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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Applicant's Amendment and remarks filed on 12/04/03 are acknowledged.

Claims 4,7 and 16-21 have been cancelled. Claim 22 has been added. Claims 1 and 8-10 have been amended. Claims 1-3, 5-6, 8-15 and 22 are currently pending in this application.

Rejection of claims 1-3, 5-6, 8-15 and 22 under 35 U.S.C. 112, second paragraph and 35 U.S.C. 103(a) is maintained for the reasons of record.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-6, 8-15 and 22 are rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention of record.

(A) The phrase "substituted with oligosaccharides" in claim 10, line 2, is a relative phrase, which renders the claim indefinite. The phrase "substituted with oligosaccharides" does not particularly point out the identity of the oligosaccharides. The specification does not provide a standard for ascertaining the requisite degree of substitution with oligosaccharide, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(B) The phrase "highly phosphorylated mannopyranosyl oligosaccharide" in claims 1 and 10 is a relative phrase, which renders the claim indefinite. The phrase "highly phosphorylated mannopyranosyl oligosaccharide" does not particularly point out the sites at which the mannopyranosyl oligosaccharide is

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phosphorylated. The specification does not provide a standard for ascertaining the requisite degree of phosphorylation of the mannopyranosyl oligosaccharide, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(C) Claims 1, 12 and 22 are vague and indefinite as it is unclear whether the phrase "chemical compound(s)" is intended to be included as a chemical compound containing carbonyl-reactive groups such as a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound or any other compound.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons of record.

Response to Arguments

Applicant's arguments filed on 12/04/03 traversing the rejection of claims 1-3, 5-6, 8-15 and 22 under 35 U.S.C. 112, second paragraph have been fully considered but they are not persuasive.

Applicant has not addressed the phrase "chemical compound" in claims 1, 12 and 22.

Applicant argues that the phrase "highly phosphorylated mannopyranosyl oligosaccharide" is defined on page 11 of the specification. It is noted that at least one M6P group is defined but applicant has not addressed the position of the phosphate groups in the rest of the highly phosphorylated mannopyranosyl oligosaccharides.

Applicant has not addressed the phrase "substituted with oligosaccharides" in claim 10.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-6, 8-15 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolvanen et al. (J.B.C., 261,20, 9546-9551, 1986) in view of Monsigny et al. (U.S. Patent 6,251,858) of record.

The claims 1-3, 5-6, 8-15 and newly added claim 22 are directed to a method for coupling a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein, which is defined as:

derivatizing the phosphorylated mannopyranosyl oligosaccharide with a chemical compound containing a carbonyl-reactive group; oxidizing the glycoprotein having at least one glycan to generate at least one aldehyde group on the glycoprotein; and reacting the oxidized glycoprotein with the derivatized phosphorylated mannopyranosyl oligosaccharide.

Additional claim limitations set forth in dependent claims include the oxidizing agent periodate or galactose oxidase; glycoprotein is a lysosomal enzyme; phosphorylated mannopyranosyl oligosaccharide contains at least one mannose 6-phosphate of the

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general formula 6-P-M_n-R and includes biantennary or triantennary mannopyranosyl oligosaccharide containing bis-M6P or tri-M6P, phosphorylated mannopyranosyl oligosaccharide can be replaced with oligosaccharides containing the terminal hexoses such as galactose, mannose, GlcNAc and fucose; the chemical compound containing carbonyl-reactive groups comprises a hydrazine, a hydrazide, an aminooxyl, or a semicarbozide compound; and a cyanoborohydride reagent to reduce the hydrazone bond.

Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates (see abstract). Tolvanen et al. disclose that a hydrazine derivative of any available carbohydrate can be introduced into oxidized cell surface glycoconjugates (see page 9546, 2nd col., 4th para.). The glycosylhydrazines of the blood group A active heptasaccharide (containing gal, GlcNAc and fucose) were coupled to periodate-oxidized cells in supplemental material col.1-2 (see coupling of glycosylhydrazines to erythrocytes and K562 cells). Tolvanen et al. also disclose the use of mannosylhydrazine in the coupling reaction (see page 9547, fig. 11 and 2nd. para.). While Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates, Tolvanen et al. differs from applicant's process in that Tolvanen et al. do not suggest the coupling of a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein such as lysosomal enzyme.

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Monsigny et al. teach the coupling of derivatives of oligosaccharides by covalent means to a protein (see abstract). Monsigny et al. discloses the biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate (see col. 16, g, lines 43-54). Monsigny et al. disclose the oligosaccharides containing the terminal hexoses such as galactose, mannose, GlcNAc and fucose (see col. 15, lines 30-50). Monsigny et al. also disclose the use of sodium cyanoborohydride to reduce the imine formed between the reducing sugar and the amine (col.3, lines 28-33). It is noted that Monsigny et al. do not suggest a method of coupling an oxidized glycoprotein with the derivatized phosphorylated mannopyranosyl oligosaccharide. Claim 22, comprises at least one mannose-6-phosphate group. Claim 22 is obvious within the prior art already set forth in the rejections of claims 1-3, 5-6, and 8-15.

Therefore, one of ordinary skill in the art would have found the applicants claimed method of coupling a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein, to have been obvious at the time the invention was made having the above cited references before him. Since Tolvanen et al. teach the coupling of glycosylhydrazines to periodate or galactose oxidase treated cell surface glycoconjugates and Monsigny et al. discloses the coupling of biantennary or triantennary mannopyranosyl oligosaccharide containing the mannose 6-phosphate to a protein, one skilled in the art would have a reasonable expectation for success in combining the process steps of the references to accomplish a method for coupling an oligosaccharide derivative by reacting with the oxidized protein wherein at least one

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glycan having at least one carbonyl group to form covalent bond conjugates. The motivation for doing so is provided by Tolvanen et al., which suggests that the glycosylhydrazines can be covalently coupled into the oxidized cell surface glycoproteins without affecting their biological activities (see page 9546, col. 2, 3rd para.).

Rejection Maintained

New claim 22 is also rejected under 35 U.S.C. 103(a) as being unpatentable over Tolvanen et al. (J.B.C., 261,20, 9546-9551, 1986) in view of Monsigny et al. (U.S. Patent 6,251,858) as already applied to claims 1-3, 5-6, and 8-15.

Response to Arguments

Applicant's arguments filed on 12/04/03 traversing the rejection of claims 1-3, 5-6, 8-15 and 22 under 35 U.S.C 103(a) have been fully considered but they are not persuasive. Applicant argues that "Tolvanen does not describe or suggest reacting an oxidized glycoprotein with a highly phosphorylated mannopyranosyl oligosaccharide compound" and "claim 1 is unobvious in light of Tolvanen in light of Monsigny". It is noted that claim 1 is directed to a method comprising derivatizing a highly phosphorylated mannopyranosyl oligosaccharide compound with a chemical compound containing at least one carbonyl-reactive group; oxidizing a glycoprotein to generate at least one carbonyl group on the glycoprotein; and reacting the said glycoprotein with the said

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oligosaccharide compound. Tolvanen teaches that a carbohydrate can be treated with hydrazine (a chemical compound containing carbonyl group) to generate a derivative such as mannosylhydrazine which is reacted with an oxidized glycoprotein wherein the glycoconjugates moiety of a glycoprotein can be oxidized with periodate to generate a carbonyl group on the glycoprotein (see the citations of the record). Monsigny teaches the M6P oligosaccharide containing glycoprotein (see citations of the record). Indeed, the examiner has established a prima facie case of obviousness rendering claims 1-3, 5-6, 8-15 and 22 rejected under 35 U.S.C. 103(a) by addressing sufficiently all of the limitations set forth in the instant claims, one skilled in the art would have a reasonable expectation for success in combining the above said references to accomplish a method for coupling a phosphorylated mannopyranosyl oligosaccharide to a glycoprotein.

2. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

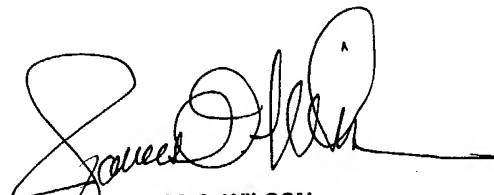
Any inquiry concerning this communication or earlier communications from the

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Examiner should be directed to Devesh Khare whose telephone number is (703)605-1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).
Art Unit 1623
April 9,2004



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600